REMARKS

Objection to the Specification

The Examiner objected to the Specification alleging that the amendment requested in the Response filed December 9, 2002 was improper and was considered by the Examiner "to be the introduction of new matter," absent an acceptable explanation.

Applicants' explanation is this: Applicants requested the removal from the specification of the source of the TONGTUT01 cDNA library, "(specimen #0065B; Mayo Clinic, Rochester MN)" This request was made pursuant to an agreement reached between the Mayo Clinic and Applicants' assignee, Incyte Pharmaceuticals, Inc. (now Incyte Corp.). That agreement requires Applicants' assignee to omit any reference to the Mayo Clinic in any of its patent applications, or else be subject to suit by the Mayo Clinic.

Applicants respectfully note that the requested ***deletion*** from the Specification of reference to the Mayo Clinic is not an introduction of "new matter" as alleged by the Examiner, and respectfully request the Examiner to cite the section(s) of the statute, rules, and/or MPEP which supports the Examiner's allegations. Otherwise, Applicants request entry of the amendment to the Specification as requested in the response filed December 9, 2002, as no new matter is added by said amendment.

Utility Rejection under 35 U.S.C. § 101 and 112, first paragraph

The rejection of claims 1, 2 and 13 is improper, as the inventions of those claims have a patentable utility as set forth in the instant specification, and/or a utility well-known to one of ordinary skill in the art. Applicants traverse this rejection for the reasons of record set forth in responses filed on January 24, 2001, February 26, 2002 and December 9, 2002 and for reasons submitted below.

At the outset, Applicants are confused by the Examiner's reference to Borrebaeck et al., and Page et al. (Office Action of July 1, 2003, page 5). At no point in this case have said references either been presented or discussed by Applicants. Therefore, said references are of no relevance in the present case.

[redacted]

Applicants request that the Examiner provide guidance as to where in Applicants arguments the Borrebaeck et al., and Page et al. papers were cited or arguments alleging the routine task of "drug discovery" by "expression profiling" were made. Absence such evidence, Applicants are left to question the Examiner's understanding of Applicants' response filed December 9, 2002 as well as the correctness of the Examiner's continued rejection of the instant application. It appears that the Examiner's arguments pertaining to the lack of utility for the instant invention lack, at least in part, applicability to the instant case.

Applicants request that the Office correct the record, in writing, to reflect that Borrebaeck et al., and Page et al. were neither cited by Applicants nor have relevance to the instant application. Additionally, absent evidence of Applicants' alleged assertion that "drug discovery" by "expression profiling" is a routine task, and such arguments by the Examiner to the contrary should also be expunged from the record.

Applicants' acknowledge the Examiner's recognition that the sequence similarity of the claimed polypeptide (SEQ ID NO:1, TCRLP) to other known T cell receptor β subunits corroborates Applicants' identification of SEQ ID NO:1 as a T-cell receptor β subunit. Therefore, Applicants will therefore confine their comments to the existence of a specific and substantial asserted utility or a well-established utility for said T cell receptor β subunit (SEQ ID NO:1) in the instant specification.

With respect to the case law present by Applicants in section I. "The Applicable Legal Standard," the cases were presented to establish the standard of utility which an Applicant must meet. As discussed in a recent Court of Appeals for the Federal Circuit case, this threshold is not high:

> An invention is "useful" under section 101 if it is capable of providing some identifiable benefit. See *Brenner v. Manson*, 383 U.S. 519, 534 [148 USPQ 689] (1966); *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 [24 USPQ2d 1401] (Fed. Cir. 1992) ("to violate Section 101 the claimed device must be ***totally incapable*** of achieving a useful result"); *Fuller v. Berger*, 120 F. 274, 275 (7th Cir. 1903) (test for utility is whether invention "is ***incapable*** of serving ***any*** beneficial end"). [Emphasis added.]

Juicy Whip Inc. v. Orange Bang Inc., 51 USPQ2d 1700 (Fed. Cir. 1999).

[redacted]

Cases such as *Fuller v. Berger, Standard Oil Co. v. Montedison, Nelson v. Bowler, In re Langer, Cross v. Iizuka* and others referred to by Applicants repeatedly affirmed that the standard of utility is *de minimis*.

Applicants wish to emphasize that this *de minimis* standard is applicable irrespective of the field of the invention. Put another way, inventions in the field of genomics are not subject to some threshold quantum of utility in excess of what is required of inventions in other fields.

Applicants again assert the polypeptides of the instant invention are useful at least in two-dimensional polyacrylamide gel electrophoresis ("2-D PAGE") analysis and western blots used to monitor protein expression and assess drug toxicity as would be understood by one of ordinary skill in the art. That these utilities are well-established is well supported by the Furness Declaration, of record. Specific and unique to the instant polypeptide include, e.g., the ability to detect the instant polypeptide; its use to detect expression levels of the instant polypeptide; and the changes in these levels in response to drug screening and toxicological assessments are specific and unique utilities to the instant polypeptide sequence.

In sum, the court has never required more than a minimum of a credible asserted utility, and it is therefore most improper for the USPTO to do so in its stead. Notwithstanding established precedent, the Examiner in effect imposes a higher standard when he asserts that the instant specification discloses no well-established specific or substantial utility.

Applicants wish to address the Examiner's assertion that the relative brevity of their disclosure regarding the use of the claimed polypeptide sequences in drug discovery techniques is evidence that such uses are not "well-established." It is an accepted tenent of patent law that a patent application does not disclose, and preferably omits, that which is well known in the art. See *In re Buchner,* 18 USPQ2d1331, 1332 (CAFC 1991). Therefore, the Examiner has employed flawed logic in concluding that Applicants' brief description regarding the utility of the claimed invention in drug screening methodologies weighs against finding that such utility is well-established.

Applicants' choice as to which techniques are described in detail and which are descirbed more summarily is irrelevant to the issue of whether an asserted utility is well-established. That classification is not assigned on the basis of what is disclosed in the specification, but rather on the basis of what is known within the relevant art.

[redacted]

Applicants note that "well-established" is distinct from "routine." In this respect, the Examiner appears to have misconstrued the point of Applicants' arguments when he alleges at page 5 that Applicants have suggested that "drug discovery" by "expression profiling" is a routine task (Office Action of July 1, 2003, page 5).

Applicants submit that no such arguments were suggested by Applicants in the instant application. Instead, their position has always been that those techniques, albeit scientifically complex, were nonetheless well-established, for the reasons already made of record.

The Office challenges Applicants' reliance on *In re Brana* on the facts of that case, alleging that the facts therein "bare *[sic]* little similarity to the facts in the instant case" (Office Action of July 1, 2003, p. 8). While it is true that the invention claimed in the instant application is of a different class of comounds from that claimed in *In re Brana*, both employed homology as evidence of utility. In *In re Brana,* the claimed antitumor compound had homology to an antitumor compound which had activity against a "particular" type of cancer, and said homology was determined to satisfy the specificity requirement. In the instant application, the claimed inventions' homology to other T cell receptor β subunit proteins of known utility would equally apply, in principle, to the instant invention. Thus, at least one of the instant inventions' utilities would be understood by the skilled artisan to be, more likely than not, to be comparable to other known T cell receptor β subunit polypeptides.

Moreover, Applicants bring to the Examiner's attention to a recent BLASTP analysis of SEQ ID NO:1 against the Genpept v136 protein database (Exhibit A). What is readily evident is that SEQ ID NO:1 and GI 1100182 (Exhibit B) share 85% sequence identity. Moreover, it has been well-established and is well known in the art that the T cell receptor beta gene cluster is located on chromosome 7 (Barker et al. (1984), Science 226:348-9, enclosed herewith, Exhibit C). Additionally, because SEQ ID NO:1 is yet another T cell receptor beta subunit protein, one of ordinary skill in the art would find it more likely than not that SEQ ID NO:1 is also located on chromosome 7. Research by O'Connor et al. (1985) Lancet I: 1295-1297 (enclosed herewith, Exhibit D) indicated the presence of gene rearrangements in the gene coding for the beta-chain of the T cell receptor in all six T cell leukemias and in 16/19 T cell lymphomas tested and provided further corroborating evidence that SEQ ID NO:1 is associated with cancers (see Specification, page 2, lines 26-28; page 43, lines 15-18). Therefore, it is more likely than not that a person of ordinary skill in the art would consider SEQ ID

[redacted]

NO:1 a T cell receptor beta subunit protein which maps to chromosome 7 and is more likely than not associated with cancer and can be used as a disease marker for T cell leukemias and T cell lymphomas. Such uses of T cell receptor beta subunit proteins including the claimed invenntion are specific, substantial and well established and well known to one of ordinary skill in the art for many years prior to Applicants' instant application.

The Examiner is correct that Applicants argue that there appear to exist differences in policy verses the law, and that the USPTO's own Training Materials require a higher standard of utility in the instant application. However, the *legal* standard of utility, as discussed above, is a *de minimus* standard. In other words, to meet the utility requirement of sections 101 and 112 of the Patent Act, the patent applicant need only show that the claimed invention is "practically useful," *Anderson v. Natta*, 480 F.2d 1392, 1397, 178 USPQ 458 (CCPA 1973) and confers a "specific benefit" on the public. *Brenner v. Manson*, 383 U.S. 519, 534-35, 148 USPQ 689 (1966). As discussed in a recent Court of Appeals for the Federal Circuit case, this threshold is not high:

> An invention is "useful" under section 101 if it is capable of providing some identifiable benefit. See *Brenner v. Manson*, 383 U.S. 519, 534 [148 USPQ 689] (1966); *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571 [24 USPQ2d 1401] (Fed. Cir. 1992) ("to violate Section 101 the claimed device must be totally incapable of achieving a useful result"); *Fuller v. Berger*, 120 F. 274, 275 (7th Cir. 1903) (test for utility is whether invention "is incapable of serving any beneficial end").

Juicy Whip Inc. v. Orange Bang Inc., 51 USPQ2d 1700 (Fed. Cir. 1999).

Therefore, Applicants maintain that the claimed invention as disclosed in the instant specification fulfills the standard of utility.

Accordingly, Applicants have established, that there is a reasonable likelihood, that the claimed polypeptides are associated with cancers and autoimmune diseases, particularly T cell leukemias and T cell lymphomas; and that one of ordinary skill in the art would find this to be so. Applicants have disclosed the claimed invention in sufficient detail and provided identifying characteristics such that the skilled artisan would know how to use the claimed invention in the research, diagnosis, treatment, and prevention of diseases associated with cancers, including T cell leukemias and T cell lymphomas, and autoimmune diseases.

Thus, for all the above reasons, the claimed polypeptide of SEQ ID NO:1 has a well-established utility and/or the Specification provides an asserted specific, substantial and credible utility. Therefore, Applicants respectfully request withdrawal of the rejection based on 35 U.S.C. §§101 and 112, first paragraph.

K. To the Extent the Rejection of the Claimed Invention Under 35 U.S.C. § 112, first paragraph, is Based on the Improper Rejection for Lack of Utility Under 35 U.S.C. § 101, it Must be Withdrawn

The rejection set forth in the Office Action is based on the assertions discussed above, i.e., that the claimed invention lacks patentable utility. To the extent that the rejection under § 112, first paragraph, is based on the improper allegation of lack of patentable utility under § 101, it fails for the same reasons.

Written Description Rejection under 35 U.S.C. §112, first paragraph,

As a preliminary matter, Applicants respectfully bring to the Examiner's attention that the Office Action mail 10/24/00 rejected both claims 1 and 2 under 35 U.S.C. §112, first paragraph alleging the inventor lacked possession of the claimed invention. However, the Office Actions mailed 4/04/01 and 9/09/02 cited this ground of rejection as only pertaining to claim 2. Applicants request clarification as to which claims stand rejected under 35 U.S.C. §112, first paragraph, for alleged lack of possession of the claimed invention. Applicants will however, in the interest of expediting prosecution and in an effort to be fully responsive, reply to this rejection as if it applied to both claims 1 and 2, though Applicants are not acquiescing in the rejection as applied to claim 1.

Claims 1 and 2 were rejected under 35 U.S.C. §112, first paragraph, allegedly because the Specification contained "subject matter which was not described in the specification in such a way as too reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention, for the reasons set forth in papers No. 7, 10, and 20, mailed 10/24/00, 4/04/01, and 9/09/02, respectively." The Office Action asserts that:

[redacted]

- [t]here is insufficient written description to show that Applicants was in possession of any variant of a peptide encoded by SEQ ID NO:1. Variant has not been defined in the specification . . . Variant is considered to include at least all "altered peptides" . . . the specification fails to disclose a representative number of species to describe the claimed genus (Office Action of October 24, 2000, page 4).

- . . . Applicant argues that the new claim language limiting the claimed protein to 90% sequence identity and IL-2 inducing activity is sufficient to overcome the previous rejection. However, said claim still encompasses a virtually unlimited number of proteins while the specification still provides an insufficient written description of said proteins. (Office Action of April 4, 2001, page 4, and Office Action of September 9, 2002, page 4).

- Applicant reiterates the disclosure . . . ***there does not appear to be any argument*** but just a reiteration of the specification. (Office Action of July 1, 2003, page 9). [emphasis added]

- [n]ote that the addition of functional language does not necessarily provide an adequate written description when the specification fails to provide any guidance as to which residues of a protein might be varied and which residues must remain constant. (Office Action of July 1, 2003, page 9).

This rejection is respectfully traversed.

Applicants reiterate their arguments filed December 9, 2002, including the references to Exhibits A and B, supplemental evidence provided by Applicants to illustrate the presence of the immunoglobulin functional domains found within TCRLP and two other TCR proteins, gi 1100182 and gi 339012. This evidence was apparently neither considered nor acknowledged by the Examiner. Clearly, it appears that the Examiner has confused this instant application and the responses filed by Applicants with those by another. Applicants respectfully request that the Examiner fully review the response filed December 9, 2002, especially pages 29-31 and the afore mentioned exhibits as it pertains to the written description rejection.

The requirements necessary to fulfill the written description requirement of 35 U.S.C. § 112, first paragraph, are well established by case law.

> . . . the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the "written description" inquiry, *whatever is now claimed. Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991)

> . . . Mention of representative compounds encompassed by generic claim language ***clearly is not required by Section 112 or any other provision of the statute***. But, where no explicit description of a generic invention is to be found in the specification...mention of representative compounds may provide an implicit description upon which to base generic claim language. *In re Robins*, 429 F.2d 452, 456-57, 166 USPQ 552, 555 (CCPA 1970) [emphasis added]

> . . . [I]t has been consistently held that the naming of one member of such a group is not, in itself, a proper basis for a claim to the entire group. However, ***it may not be necessary to enumerate a plurality of species if a genus is sufficiently identified in an application by 'other appropriate language.'*** *In re Grimme*, 274 F.2d 949, 952, 124 USPQ 499, 501 (CCPA 1960) [emphasis added]

Attention is also drawn to the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001, which provide that:

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., ***complete or partial structure***, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. ***If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met.*** [emphasis added] [footnotes omitted]

Thus, the written description standard is fulfilled by both what is specifically disclosed and what is conventional or well known to one skilled in the art.

I. The specification provides an adequate written description of the claimed "variants" of SEQ ID NO:1

[redacted]

The subject matter encompassed by Claims 1 and 2 are either disclosed by the specification or conventional or well known to one skilled in the art.

With respect to the rejection as it applies to independent claim 1, that claim recites "A purified T-cell receptor beta-like protein comprising the amino acid sequence of SEQ ID NO:1." Applicants' believe, based on the Examiner's withdrawal of the rejection under 35 U.S.C. § 101 (in which the Examiner states, "the protein encoded by Applicant's combined ESTs is not likely a T cell receptor β subunit, has been withdrawn" (Office Action of July 1, 2003, page 2)), that a rejection of claim 1 under 35 U.S.C. §112, first paragraph for an alleged inadequate written description is also moot.

With respect to the rejection as it applies to idependent claim 2, that claim recites "A variant of T-cell receptor beta-like protein having at least 90% amino acid identity to SEQ ID NO:1 and which retains IL-2 inducing activity." The Examiner's position is based upon the theory that the Specification provides an adequate written description of SEQ ID NO:1, however, the Specification allegedly lacks an adequate written description of the variant polypeptides because, "the specification fails to provide any guidance as to which residues of a protein might be varied and which residues must remain constant" (Office Action of July 1, 2003 at page 9). Applicants strongly disagree with this position.

Such a position ignores that the polypeptides recited in claim 2) ***are*** described in terms of their structure. That is, the claimed polypeptides are "***at least 90% identical to the amino acid sequence of SEQ ID NO:***1." The structure of SEQ ID NO:1 is provided in the specification, for example, at pages 53-55 of the Sequence Listing and Figures 1A, 1B, 1C and 1D for SEQ ID NO:1. The phrases "percent identity" or "% identity" as well as methods for determining such identity are well known to the skilled artisan. Claim 2, as previously amended, does not encompass any peptide or protein with altered sequence, but rather is limited to those having at least 90% amino acid sequence identity to SEQ ID NO:1, and which retain a specified biological function of a T-cell receptor protein, namely the ability to induce IL-2 activity.

Applicants submit that this description is sufficient to describe the claimed genus based on the disclosure of the single species, SEQ ID NO:1, for reasons stated in the USPTO's own training materials for implementation of the Written Description Guidelines under 35 U.S.C. § 112, first paragraph. In the "Synopsis of Application of Written Description Guidelines" (USPTO Website www.uspto.gov, March 1, 2000), at page 53 of these guidelines, a claim to "A protein having SEQ ID

NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A → B" is considered to meet the written description requirements because:

> --- procedures for making variants of SEQ ID NO:3 are conventional in the art and an assay is described which will identify all other proteins having the claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO:3 which have 95% identity to SEQ ID NO:3 and retain its activity are conventional in the art.

The Guidelines further state:

> The single species disclosed (SEQ ID NO:3) is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO:3 which are capable of the specified catalytic activity.

A detailed description of the chemical and structural features of SEQ ID NO:1 which contribute to the characterization of SEQ ID NO:1 and other related proteins associated with T cell receptor beta subunits are provided, for example, at page 14, lines 16-23 and Figures 2A and 2B. Ninety percent variants of the claimed polypeptides are described, for example, at page 14, lines 26-30 and an assay to identify 90% variants having IL-2 inducing activity is provided in the Specification, Example X (Specification, page 50, line 21 to page 51, line 5).

When provided with the detailed description as noted above, one of ordinary skill in the art "would have understood the inventor to be in possession of the claimed invention at the time of filing." That is, one of ordinary skill in the art would recognize polypeptide sequences which are variants at least 90% identical to SEQ ID NO:1. Given a polypeptide sequence, it would be routine for one of skill in the art to recognize whether it was a variant of SEQ ID NO:1 and to determine the % identity to SEQ ID NO:1 of the variant. Accordingly, the specification provides an adequate written description of the recited variants of SEQ ID NO:1.

II. The specification provides an adequate written description as required by law

Applicants submit that case law in the area of the written description requirement of 35 U.S.C. 112, first paragraph is clear with regard to the details considered sufficient to describe a claimed genus:

> . . . Mention of representative compounds encompassed by generic claim language ***clearly is not required by Section 112 or any other provision of the statute***. But, where no explicit description of a generic invention is to be found in the

> specification . . . mention of representative compounds may provide an implicit description upon which to base generic claim language. *In re Robins*, 429 F.2d 452, 456-57, 166 USPQ 552, 555 (CCPA 1970) [emphasis added]
>
> . . . [I]t has been consistently held that the naming of one member of such a group is not, in itself, a proper basis for a claim to the entire group. However, ***it may not be necessary to enumerate a plurality of species if a genus is sufficiently identified in an application by 'other appropriate language.'*** *In re Grimme*, 274 F.2d 949, 952, 124 USPQ 499, 501 (CCPA 1960) [emphasis added]

The specification sets forth a description of the claimed polypeptide variants using "other appropriate language" as indicated above in connection with the remarks regarding an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO:1". The claimed variants have been described in terms of their relationship to the chemical structure of SEQ ID NO:1 and structural requirements at, for example, pp. 53-55 of the Sequence Listing; Figures 1A, 1B, 1C, and 1D; page 14, lines 16-23 and Figures 2A and 2B. The specification provides a means of identifying functional variants having 90% sequence identity with SEQ ID NO:1 at, for example, page 14, lines 26-30 and the assay taught in Example X (Specification, page 50, line 21 to page 51, line 5). Applicants therefore submit that the "genus is sufficiently identified in [the instant] application by 'other appropriate language'" as stated in *In re Grimme*, 274 F.2d 949, 952, 124 USPQ 499, 501 (CCPA 1960). Furthermore, Applicants submit that "a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing" as stated in the Patent and Trademark Office's own "Guidelines for Examination of Patent Applications Under the 35 U.S.C. Sec. 112, para. 1", published January 5, 2001. Accordingly, Claims 1 and 2 meets the statutory requirements for written description under 35 U.S.C. 112, first paragraph.

III. Conclusion

The Final Office Action failed to base its written description inquiry pertinent to Applicants' rebuttal submitted December 9, 2002. Consequently, the Action did not provide an appropriate analysis of Applicants rebuttal mailed December 9, 2002 and the present claims in view of their scope. In particular, the subject matter of the claims of the instant application is defined in terms of the chemical

structure of SEQ ID NO:1. The courts have stressed that structural features are important factors to consider in a written description analysis of claims to nucleic acids and proteins. In addition, the genus of polypeptides defined by the present claims is adequately described, as evidenced by specific passages of the specification as set forth above. Furthermore, the Examiner has applied to the subject application a written description standard that has no basis in the law.

For at least the above reasons it is believed that Claims 1 and 2 meet the written description requirement of 35 U.S.C. § 112, first paragraph. It is therefore requested that this rejection be withdrawn.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding objections/rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned at the number listed below.

Please charge Deposit Account No. **09-0108** in the amount of **$ 110.00** as set forth in the enclosed fee transmittal letter. If the USPTO determines that an additional fee is necessary, please charge any required fee to Deposit Account No. 09-0108.

Respectfully submitted,

INCYTE CORPORATION

Date: 03 November 2003

Shirley A. Recipon
Reg. No. 47,016
Direct Dial Telephone: (650) 621-8555

Date: November 2003

Cathleen M. Rocco
Reg. No. 46,172
Direct Dial Telephone: (650) 845-4587

Customer No.: 27904
3160 Porter Drive
Palo Alto, California 94304
Phone: (650) 855-0555
Fax: (650) 849-8886

Attachment(s):

Exhibit A: BLASTP analysis of SEQ ID NO:1 against the Genpept v136 protein database
Exhibit B: GI 1100182
Exhibit C: Barker et al. (1984), Science 226:348-9
Exhibit D: O'Connor et al. (1985) Lancet I:1295-1297